

HFA- 305
Dockets mgmt. branch

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FREEDOM OF INFORMATION SUMMARY

NADA 096-298

BOVATEC® (lasalocid) Type A Medicated Article

"For increased rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers)."

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

Sponsored By:

Alpharma Inc.
One Executive Drive
Fort Lee, NJ 07024

NADA 96-298

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FREEDOM OF INFORMATION SUMMARY

Bovatec® for Pasture Cattle

I. GENERAL INFORMATION

NADA: 96-298

Sponsor: Alpharma Inc.
One Executive Drive
Fort Lee, NJ 07024

Established Name: Lasalocid

Trade Name: BOVATEC®

Marketing Status: OTC

EFFECT OF SUPPLEMENT:

21 CFR 558.311 currently provides for the use of lasalocid (1) to improve feed efficiency and increase rate of weight gain in cattle fed in confinement for slaughter, (2) to increase rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers) when fed daily in at least one pound of supplemental feed, and (3) to increase rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers) when lasalocid is provided in a free-choice supplemental feed.

The Animal Drug Availability Act of 1996 (ADAA) eliminated the requirement for dose optimization of a new animal drug. A dose or dose range is approvable up to a maximal dose that has been shown not to cause human or target animal safety concerns and does not depress animal response to the drug below that of the most efficacious dose [*Federal Register* 62(214):59832]. Based upon this provision, the effect of this supplement is to provide for free-choice and hand-fed consumption of lasalocid at a rate of not less than 60 mg nor more than 300 mg per head per day to increase rate of weight gain in pasture cattle as described in the following sections.

II. INDICATIONS FOR USE

For increased rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers).

III. DOSAGE FORM, DOSAGE, AND ADMINISTRATION

Bovatec medicated premix:

- Bovatec® 20 Liquid, liquid premix containing 90.7 g lasalocid sodium activity per pound.
- Bovatec® 68, dry premix containing 68 g lasalocid sodium activity per pound.
- Bovatec® 150, dry premix containing 150 g lasalocid sodium activity per pound.

Bovatec Dosage:

Use Level	Indications for Use
Feed continuously in a free-choice or hand-fed supplemental feed to provide not less than 60 nor more than 300 mg/head/day. Daily lasalocid intakes in excess of 200 mg/head/day have not been shown to be more effective than 200 mg lasalocid/head/day. For hand-fed use, the drug must be contained in at least 1 pound of supplement.	For increased rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers) when fed in a free-choice or hand-fed supplemental feed.

IV. EFFECTIVENESS:

For Cattle Hand-Fed:

Summary of Efficacy Data (*As previously described in FOI Summary Dated April, 1984 for Bovatec for Pasture Cattle: 49 FR December 20, 1984, p. 49449 approval.*)

Fifteen well controlled replicated studies were conducted in slaughter, stocker, and feeder cattle on pasture in 12 different states. Duration of the studies ranged from 84 to 142 days with an average of 107 days. Steers were fed in 12 studies and heifers were fed in 3 studies. At the beginning of the study, animal weights ranged from 300 to 947 pounds and averaged 568 pounds. Each study contained replicates of nonmedicated control animals for comparison purposes.

Statistical Analysis

Analysis of variance was conducted on each study, considering the 0, 50, 100, 200, and 300 mg lasalocid treatments. The estimated treatment study means were pooled in an analysis of variance which included terms for an overall mean, treatment, location, and study within location. Each treatment-study mean was weighted by the number of replications contributing to that mean. The lower end of the statistically effective treatment dose was determined by non-overlapping confidence intervals on the predicted responses at

0, 50, and 100 mg/head/day Bovatec at the 0.95 level of confidence. The upper end of the range was determined by a linear plateau model for the treatment means.

Results of Efficacy Studies

From the pooled analysis of the fifteen pasture studies, the estimated treatment means for average daily gain (ADG) are as follows:

Control	1.26 lb/day
50 mg Bovatec	1.27 lb/day
100 mg Bovatec	1.32 lb/day
200 mg Bovatec	1.40 lb/day
300 mg Bovatec	1.42 lb/day

Average daily gain results from the pooling of the fifteen studies indicate that the one-sided 95% confidence interval on the predicted response at 0 mg/head/day Bovatec did not overlap the corresponding confidence interval at 60 mg/head/day Bovatec. The linear plateau model indicated a linear trend in average daily gain response over the interval 0 to 200 mg/head/day Bovatec with no statistical improvement in average daily gain from 200 to 300 mg/head/day Bovatec. In summary, the overall analysis of these fifteen field studies indicates that when Bovatec is incorporated in the grain supplement to slaughter, stocker, or feeder cattle between 60 and 200 mg/head/day, the cattle had a significant ($P < 0.05$) improvement in gain over cattle fed the grain supplement without Bovatec.

Details and Results of the Individual Studies

Study C-50

This study was conducted at the University of Missouri Research Farm, Columbia, Missouri, by Dr. J. A. Paterson and Dr. D. K. Bowman, Department of Animal Science, College of Agriculture, University of Missouri, Columbia, Missouri.

Forty-three steers, average initial weight 484 pounds, were fed for 112 days on fescue pasture. Only those treatments will be reported which relate to this claim. Each treatment was replicated three times with five animals per replicate.

	<u>Control</u>	<u>Bovatec 200 mg/head/day</u>
ADG (lb)	1.12	0.98

Study C-51

This study was conducted at the University of Arkansas Beef Substation at Newport, Arkansas, by Dr. J. W. Spears, Department of Animal Science, College of Agriculture, University of Arkansas, Fayetteville, Arkansas.

Sixty-four steers, average initial weight 476 pounds, were fed for 113 days on fescue pasture. Only those treatments will be reported which relate to this claim. Each treatment was replicated two times with eight animals per replicate.

	<u>Control</u>	<u>Bovatec 100 mg/head/day</u>	<u>Bovatec 200 mg/head/day</u>
ADG (lb)	0.94	0.95	0.94

Study C-62

This study was conducted at the University of Missouri Research Farm, Columbia, Missouri, by Dr. J. A. Paterson, Department of Animal Science, College of Agriculture, Columbia, Missouri.

Fifty steers, average initial weight 464 pounds, were fed for 105 days on tall fescue pasture. The carrier for the drug was either soybean oil meal or dehydrated alfalfa + distillers dried grains. Each treatment was replicated two times with five animals per replicate.

		<u>Soybean Oil Meal</u>		<u>Dehydrated Alfalfa + Distillers Dried Grains</u>	
	<u>Control</u>	<u>Bovatec 0 mg/head/day</u>	<u>Bovatec 200 mg/head/day</u>	<u>Bovatec 0 mg/head/day</u>	<u>Bovatec 200 mg/head/day</u>
ADG (lb)	0	0.94	1.10	1.05	1.15

Study C-79

This study was conducted at Kansas State University Research Farms, Manhattan, Kansas, by Dr. L. Corah and Dr. J. G. Riley, Department of Animal Science, College of Agriculture, Kansas State University, Manhattan, Kansas.

Eighty-eight steers, average initial weight 557 pounds, were fed for 100 days on brome grass pasture. Each treatment was replicated four times with two replicates containing four animals and two replicates containing seven animals in each treatment.

	<u>Control</u>	<u>Bovatec 100 mg/head/day</u>	<u>Bovatec 200 mg/head/day</u>	<u>Bovatec 300 mg/head/day</u>
ADG (lb)	2.17	2.24	2.37	2.24

Study C-80

This study was conducted at Middle Tennessee Experiment Station, Springhill, Tennessee, by Dr. J. W. Holloway and Dr. J. W. High, Department of Animal Science, University of Tennessee, Knoxville, Tennessee.

Seventy-two heifers, average initial weight 625 pounds, were fed for 84 days on fescue pasture. Each treatment was replicated five times with three animals per replicate. Only those treatments will be reported which were included in the pooled analysis.

	<u>Control</u>	<u>Lasalocid 50</u> <u>mg/head/day</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>
ADG (lb)	1.37	1.37	1.45

Study C-84

This study was conducted at the University of Arkansas Beef Substation, Newport, Arkansas, by Dr. J. W. Spears, Department of Animal Science, College of Agriculture, University of Arkansas, Fayetteville, Arkansas.

Eighty-four steers, average initial weight 758 pounds, were fed for 90 day on a) tall fescue – white clover – bermudagrass, b) rye-ryegrass – arrowleaf clover – bermudagrass, and c) wheat – ryegrass – arrowleaf clover – bermudagrass pastures. Each treatment was replicated three times with seven animals per replicate.* All animals received a total of six pounds of grain per head per day for the first 45 days of the study and 10 pounds per head per day during the remainder of the study. Cattle were slaughtered directly off the pasture study.

* One replicate of each treatment was pastured on each pasture type (a, b, or c).

	<u>Control</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>	<u>Lasalocid 200</u> <u>mg/head/day</u>	<u>Lasalocid 300</u> <u>mg/head/day</u>
ADG (lb)	1.42	1.47	1.65	1.65

Study C-91

This study was conducted at North Carolina State University Animal Science Research Farm, Raleigh, North Carolina, by Dr. J. W. Spears, Department of Animal Science, College of Agriculture, North Carolina State University, Raleigh, North Carolina.

Seventy-two steers, average initial weight of 658 pounds were fed for 126 days on tall fescue, orchardgrass, and ladino clover pastures. Each treatment was replicated three times with eight animals per replicate.

	<u>Control</u>	<u>Lasalocid 200</u> <u>mg/head/day</u>	<u>Lasalocid 300</u> <u>mg/head/day</u>
ADG (lb)	1.11	1.32	1.26

Study C-92

This study was conducted at Dunmor, Kentucky, by Dr. N. Bradley, Lexington, Kentucky.

Sixty-four steers, average initial weight of 458 pounds, were fed for 112 days on grass-clover mixed pastures. Each treatment was replicated two times with eight animals per replicate.

	<u>Control</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>	<u>Lasalocid 200</u> <u>mg/head/day</u>	<u>Lasalocid 300</u> <u>mg/head/day</u>
ADG (lb)	1.06	1.10	1.13	1.14

Study C-94A

This study was conducted at the Moorman Manufacturing Co. Beef Research Farm, Mindon, Illinois, by Dr. Albert Peter, Moorman Manufacturing Co., Quincy, Illinois.

Eighty steer calves, average initial weight 518 pounds, were fed for 112 days on alfalfa-orchardgrass pasture. Each treatment was replicated two times with ten animals per replicate.

	<u>Control</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>	<u>Lasalocid 200</u> <u>mg/head/day</u>	<u>Lasalocid 300</u> <u>mg/head/day</u>
ADG (lb)	1.08	1.10	1.19	1.27

Study C-102

This study was conducted at the University of Florida Experiment Station Ona, Ona, Florida, by Dr. Glyn Horton, Department of Animal Science, Ona Experiment Station, Ona, Florida.

One hundred ninety-two heifers, average initial weight 528 pounds, were fed for 112 days on Ona stargrass pastures. Each treatment was replicated three times with 16 animals per replicate.

	<u>Control</u>	<u>Lasalocid 50</u> <u>mg/head/day</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>	<u>Lasalocid 200</u> <u>mg/head/day</u>
ADG (lb)	0.99	1.04	1.05	1.15

Study C-103

This study was conducted at Southeastern Kansas Experiment Station, Kansas State University, Parsons, Kansas, by Dr. Lyle Lomas, Department of Animal Science, Kansas State University, Parsons, Kansas.

Seventy-two steers, average initial weight of 642 pounds, were fed for 112 days on smooth brome grass pastures. Each treatment was replicated three times with eight animals per replicate.

	<u>Control</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>	<u>Lasalocid 200</u> <u>mg/head/day</u>
ADG (lb)	1.34	1.55	1.66

Study C-156

This study was conducted at the Animal Science Research Farm, South Dakota State University, Brookings, South Dakota, by Dr. Lawrence Embry, Department of Animal Science, College of Agriculture, South Dakota State University, Brookings, South Dakota.

Sixty-four steers, average initial weight 686 pounds, were fed for 142 days on a brome-grass-alfalfa pasture. Each treatment was replicated four times with four animals per replicate.

	<u>Control</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>	<u>Lasalocid 200</u> <u>mg/head/day</u>	<u>Lasalocid 300</u> <u>mg/head/day</u>
ADG (lb)	1.33	1.28	1.39	1.56

Study C-171

This study was conducted at the Horton Feedlot and Research Center, Wellington, Colorado, by Dr. Dallas Horton, Horton Feedlot and Research Center, Wellington, Colorado.

Ninety-six heifers, average initial weight 509 pounds, were fed for 98 days on brome and western wheat grass pastures. Each treatment was replicated four times with eight animals per replicate.

	<u>Control</u>	<u>Lasalocid 50</u> <u>mg/head/day</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>
ADG (lb)	1.42	1.51	1.53

Study C-172

This study was conducted at the Simpson Experiment Station, Pendleton, South Carolina, by Dr. D. L. Cross, Department of Animal Science, College of Agriculture, Clemson University, Clemson, South Carolina.

Sixty-three steers, average initial weight 557 pounds, were fed for 98 days on bermudagrass pastures. Each treatment was replicated three times with seven animals per replicate.

	<u>Control</u>	<u>Lasalocid 50</u> <u>mg/head/day</u>	<u>Lasalocid 100</u> <u>mg/head/day</u>
ADG (lb)	1.16	1.15	1.23

Study C-185

This study was conducted at the Oregon State University Research Farms (Soap Creek Ranch and Berry Creek Ranch), Corvallis, Oregon, by Dr. Dale Weber, Department of Animal Science, College of Agriculture, Oregon State University, Corvallis, Oregon.

Sixty steers, average initial weight 610 pounds, were fed for 91 days on subterranean clover, tall fescue and rye grass pastures. The study was conducted in two blocks with three treatments per block. Each treatment was replicated two times with five animals per replicate.

	<u>Control</u>	<u>Lasalocid 50 mg/head/day</u>	<u>Lasalocid 100 mg/head/day</u>
ADG (lb)	1.07	1.12	1.25

For Cattle Fed Free-Choice:

Summary of Efficacy Data *(As previously described in FOI Summary Dated December 2, 1985 for Bovatec for Pasture Cattle Fed on a Free-Choice Basis: 51 FR February 12, 1986, p. 5162-3 approval.)*

A total of 566 stocker and feeder cattle were used in nine replicated well-controlled studies on pastures in eight different states. Each study contained replicates of nonmedicated control animals for comparison purposes. Duration of the studies ranged from 84 to 112 days. Steers were used in all studies. Two pens of heifers were included in one study. A total of 306 animals received lasalocid in free-choice supplements and their rate of weight gain was compared to the rate of weight gain for 260 nonmedicated control animals. At the beginning of the studies, animal weights ranged from 436 to 848 pounds and averaged 597 pounds. Thirty-six medicated animals from two additional studies were included in the determination of average lasalocid intake and in establishing the coefficient of variation for lasalocid intake.

The initial approval for free-choice lasalocid consumption for pasture cattle did not contain provision for use in dairy and beef replacement heifers. Approval of free-choice lasalocid for dairy and beef replacement heifers was covered in a FOI Summary dated March 1987. Safety data presented in that FOI Summary remain the basis for inclusion of these classes of cattle in the free-choice lasalocid approval.

Statistical Analysis

An analysis of variance (ANOVA) was made for each study, using the average daily gain (AGD) results from both the control and Bovatec-treated groups. The variances of individual studies were found to be homogeneous (Barlett's test), and ADG results from the nine studies were pooled for an overall analysis. Treatment difference was determined using a two-tailed t-test. The consumption data, reported as average intake of Bovatec in mg per head per day (mg/hd/day), from the medicated replications in all eleven studies were evaluated for each 14-day period. These data were used to establish average lasalocid intake for each study and in making an estimation of the variance in average lasalocid intake between 14-day periods within the studies. The amount of variation in lasalocid intake was then described as a percentage of average lasalocid intake by calculating a Coefficient of Variation (C.V.).

Results

From the pooled analysis of the nine pasture studies, the estimated treatment means for average daily gain (ADG) are as follows:

Control	1.540 lb/day
Bovatec Medicated Supplements	1.602 lb/day

In summary, the overall analyses of these nine field studies indicate that when Bovatec was fed to slaughter, stocker or feeder cattle on pasture in free-choice supplemental feeds, these cattle had significant ($P=0.036$) improvement in rate of gain over cattle fed the supplements without Bovatec. Further, Bovatec was effective when received by the treated cattle with variation in average daily intake, which produced a Coefficient of Variation of 35.08%.

Details and Results of the Individual Studies

Study C-94-B

This study was conducted at Moorman Beef Research Farm, Moorman Manufacturing Co., Quincy, Illinois, by Dr. A. P. Peter, Manager, Beef Cattle Research, Moorman Manufacturing Co., Quincy, Illinois.

Ninety steers, average initial weight 512 pounds, were fed for 98 days on alfalfa-orchardgrass pastures. Each treatment was replicated three times with ten animals per replicate.

	<u>Control</u>	<u>Bovatec, as Lasalocid, g/t</u> <u>(3 reps 4000) – (3 reps 6000)</u>
ADG (lb)	0.66	0.80
Bovatec (mg/hd/day)	0.0	197.1

Study C-154

This study was conducted at the Moorman Beef Research Farm, Moorman Manufacturing Co., Quincy, Illinois, Dr. A. P. Peter, Manager, Beef Cattle Research, Moorman Manufacturing Co., Quincy, Illinois.

Forty-eight steers, average initial weight 498 pounds, were fed for 84 days on alfalfa-bromegrass pastures. Each treatment was replicated two times with eight animals per replicate.

	<u>Control</u>	<u>Bovatec, as Lasalocid, g/t</u> <u>(2 reps 1440) – (2 reps 2880)</u>
ADG (lb)	1.61	1.80
Bovatec (mg/hd/day)	0.0	187.2

Study C-84-29

This study was conducted at Oregon State University, Corvallis, Oregon, by Dr. Dale Weber, Department of Animal Science, Oregon State University, Corvallis, Oregon.

Forty-two stocker cattle (14 heifers, 28 steers) average initial weight 652 pounds, were fed for 84 days on meadow foxtail, subterranean clover, tall fescue and perennial ryegrass pastures. Each treatment was replicated three times with seven animals per replicate.

	<u>Control</u>	<u>Bovatec, as Lasalocid, 1440 g/t</u>
ADG (lb)	2.59	2.70
Bovatec (mg/hd/day)	0.0	148.4

Study C-84-30

This study was conducted at the University of Kentucky, College of Agriculture Research Farms, Lexington, Kentucky, by Dr. James A. Boling, Department of Animal Science, University of Kentucky, Lexington, Kentucky.

Sixty-four steers, average initial weight 594 pounds, were fed for 98 days on tall fescue-Kentucky bluegrass pastures. Each treatment was replicated four times with eight animals per replicate.

	<u>Control</u>	<u>Bovatec, as Lasalocid, 1440 g/t</u>
ADG (lb)	1.19	1.17
Bovatec (mg/hd/day)	0.0	102.1

Study C-84-31

This study was conducted at the Coastal Plains Experiment Station, Tifton, Georgia, by Dr. P. R. Utley and G. M. Hill, University of Georgia, Coastal Plains Experiment Station, Tifton, Georgia.

Fifty steers, average initial weight 681 pounds, were fed for 98 days on bahiagrass pastures. Each treatment was replicated five times with five animals per replicate.

	<u>Control</u>	<u>Bovatec, as Lasalocid, 1440 g/t</u>
ADG (lb)	1.07	1.22
Bovatec (mg/hd/day)	0.0	161.9

Study C-84-32

This study was conducted at the Simpson Agricultural Station, Clemson, South Carolina, by Dr. Dee L. Cross, Department of Animal Science, Clemson University, Clemson, South Carolina.

Sixty-four steers, average initial weight 667 pounds, were fed for 98 days on fescue and bermudagrass pastures. Each treatment was replicated four times with eight animals per replicate.

	<u>Control</u>	<u>Bovatec, as Lasalocid, 1440 g/t</u>
ADG (lb)	0.60	0.69
Bovatec (mg/hd/day)	0.0	113.2

Study C-84-34

This study was conducted at Johnson Farms, Parma, Idaho, by Dr. E. G. Johnson, Parma, Idaho.

Eighty steers, average initial weight 622 pounds, were fed for 98 days on irrigated alta fescue pastures. Each treatment was replicated five times with eight animals per replicate.

	<u>Control</u>	<u>Bovatec, as Lasalocid, 1440 g/t</u>
ADG (lb)	1.74	1.66
Bovatec (mg/hd/day)	0.0	199.4

Study C-84-35

This study was conducted at Hoffman-La Roche, Inc., Animal Science Research Experiment Farm, Wrightstown, New Jersey, by Mr. Howard Eisenbeis, Wrightstown, New Jersey.

Sixty-four steers, average initial weight 610 pounds, were fed for 112 days on ryegrass, bromegrass, orchardgrass, clover and alfalfa mix pastures. Each treatment was replicated four times with eight animals per treatment.

	<u>Control</u>	<u>Bovatec, as Lasalocid, 1440 g/t</u>
ADG (lb)	2.49	2.57
Bovatec (mg/hd/day)	0.0	186.9

Study C-84-36

This study was conducted at the University of Florida, Agricultural Research and Educational Center, Ona, Florida, by Dr. David Sanson, University of Florida, Ona, Florida.

Sixty-four steers, average initial weight 619 pounds, were fed for 98 days on Ona stargrass pastures. Each treatment was replicated four times with eight steers per replicate.

	<u>Control</u>	<u>Bovatec, as Lasalocid, 1440 g/t</u>
ADG (lb)	1.55	1.51
Bovatec (mg/hd/day)	0.0	156.7

V. SAFETY FOR THE TARGET SPECIES

For Cattle Hand-Fed:

The target animal safety for the administration of 300 mg/head/day lasalocid to slaughter, stocker, and feeder cattle on pasture is described in FOI Summary Dated April, 1984 for Bovatec for Pasture Cattle: 49 FR December 20, 1984, p. 49449 approval. Two animal safety studies were conducted in which pasture cattle were offered 200, 600, and 1000 mg of lasalocid per head daily in one pound of grain for 90 or 98 days. No toxic effects were reported in either study, and the data indicated that lasalocid was safe at five times the proposed dosage (5 X 200 mg/head/day).

For Cattle Fed Free-Choice:

The target animal safety for the administration of 300 mg/head/day lasalocid on a free-choice basis to slaughter, stocker, and feeder cattle on pasture is described in FOI Summary Dated December 2, 1985 for Bovatec for Pasture Cattle Fed on a Free-Choice Basis: 51 FR February 12, 1986, p. 5162-3 approval. Three hundred forty-two cattle from the studies used in determining average daily drug intake were exposed to lasalocid in self-fed pasture supplements with concentrations of 1440 to 6000 g/t for periods of 84 to 112 days. No adverse reactions or dangerously excessive intakes were noted. The highest average daily intake of lasalocid for any group of cattle for one 14-day period was 596 mg per head, and intake decreased in the following periods. It was concluded that the addition of lasalocid to self-fed supplements for cattle on pasture is safe for use at various concentrations.

VI. HUMAN SAFETY

An FOI Summary was prepared with a supplemental application to NADA 96-298, approved 8/6/1982, providing for the use of lasalocid in complete feeds for cattle in confinement at the rate of 100-360 mg per head daily as detailed in 21 CFR Section 558.311. The current application is for use of lasalocid premixes for hand-feeding, or to formulate various free-choice supplemental feeds, to provide lasalocid intakes of 60 to 300 mg/head/day on a nonconfined basis; therefore, the previous FOI Summary covers the toxicity, safe concentrations of residues, metabolism, total residues, and regulatory method aspects for the use of lasalocid for nonconfined cattle.

VII. AGENCY CONCLUSIONS:

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrates that 60-300 mg lasalocid/head/day when used in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers) is safe and effective for increased rate of weight gain. However, intakes of lasalocid in excess of 200 mg/head/day have not been shown to be more effective than 200 mg/head/day.

The Center for Veterinary Medicine has concluded that, for this product, adequate directions for use by the layman have been provided. Historically, the industry is familiar with the handling and mixing of Type A medicated articles into Type B and C medicated feeds. Lasalocid is not a controlled substance. Thus, labeling is adequate for the intended use.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval for food producing animals does not qualify for marketing exclusivity because the supplemental application does not contain substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) required for the approval and conducted or sponsored by the applicant.

VIII. LABELING

The following labeling is attached:

1. Bovatec ® 68 (dry Type A Medicated Article)
2. Bovatec ® 150 (dry Type A Medicated Article)
3. Bovatec ® Liquid 20 (liquid Type A Article)
4. Blue Bird Lasalocid (Cattle Hand-Fed Supplement)
5. Blue Bird M (Ruminant Free-Choice Mineral and Vitamin Supplement)
6. Blue Bird L (Ruminant Free-Choice Mineral and Vitamin Supplement - Liquid)

CONTROL NO.:
EXPIRATION DATE:

ALPHARMA
Animal Health Division

Bovatec®

68

Bovatec® 68

Bovatec
68

Lasalocid sodium
Type A Medicated Article
(medicated premix)

See back panel for use directions.

Net wt 50 LB (22.68 kg)



ALPHARMA
Animal Health Division

ALPHARMA
Animal Health Division

Bovatec[®]
68

Lasalocid sodium
Type A Medicated Article
(medicated premix)

[illegible]

Bag size: 16.5" x 5" x 38"

900000

CONTROL NO.:
EXPIRATION DATE:

ALPHARMA
Animal Health Division

Bovatec
150 EP

Bovatec®

150 FP

Bovatec
150 FP

Lasalocid sodium
Type A Medicated Article
(medicated premix)

See back panel for use directions.

Net wt 50 LB (22.68 kg)

ALPHARMA
Animal Health Division

Bovatec
150 FP

Lasalocid sodium
Type A Medicated Article
(medicated premix)

[illegible]

Bag size: 16.5" x 4.5" x 38"

Lasalocid sodium Type A Medicated Article (medicated premix)

Active Ingredient

(each pound contains 150 grams (33.1%) of lasalocid (as lasalocid sodium active) in a carrier suitable for incorporation in feed.

Mixing directions

This product should be further diluted in an intermediate blending step prior to mixing in final feed. **Do not feed undiluted.**

A. Feedlot cattle being fed in confinement for slaughter - For improved feed efficiency and increased rate of weight gain and for control of coccidiosis caused by *Eimeria bovis* and *E. zuernii*.
Sheep - For prevention of coccidiosis caused by *Eimeria ovinis*, *E. crandalli*, *E. ovivalidis* (*E. nimishahajemae*), *E. parva* and *E. stiedae* in sheep maintained in confinement.

Feeding directions

For improved feed efficiency in cattle:
Feed continuously at the rate of not less than 10 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 100 mg nor more than 300 mg per head per day.
For improved feed efficiency and increased rate of weight gain in cattle:
Feed continuously at the rate of not less than 10 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 100 mg nor more than 300 mg per head per day.
For control of coccidiosis in cattle:
Feed continuously at the rate of 30 grams of lasalocid per ton of total ration (90% dry matter) to provide an intake of 1 mg of lasalocid per 2.2 pounds of body weight per day or cattle up to 800 pounds (maximum 300 mg per day).
For prevention of coccidiosis in sheep:
Feed continuously at the rate of not less than 20 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 15 mg nor more than 20 mg per head per day depending on body weight.

1. Complete feeds for feedlot cattle and sheep in confinement

a. Intermediate blending: Mix 1 part of Bovatec 150 FP premix (Type A Medicated Article) with 29 parts of finely ground non-medicated feedstuffs to provide an intermediate premix containing 5 grams of lasalocid per pound.
b. Using this intermediate premix, the following table would apply to the manufacture of complete feeds:

Intended lasalocid concentration in the complete feed:	Add the following amounts of 5 grams per pound intermediate premix per ton of complete feed mixed:	
<u>grams/ton</u>	<u>mg/lb</u>	<u>pounds/ton</u>
10	5	2
20	10	4
25	12.5	5
30*	15	6

*Maximum approved concentration in complete feeds.

2. Supplements for feedlot cattle and sheep in confinement

a. Dry supplements
(1) Intermediate blending: Mix 1 part of Bovatec 150 FP premix (Type A Medicated Article) with 6.5 parts of finely ground non-medicated feedstuffs to provide an intermediate premix containing 20 grams of lasalocid per pound.
(2) Using this intermediate premix, the following table would apply to the manufacture of feedlot supplements:

Feedlot supplements		
Intended lasalocid concentration in the supplement:	Add the following amounts of 20 grams per pound intermediate premix per ton of supplement mixed:	
quantity	mg/lb	quantity
100	50	5
200	100	10
300	150	15
360	180	18
400	200	20
500	250	25
600	300	30
720	360	36
800	400	40
1200	600	60
1440	720	72

(3) Thoroughly mix supplement with grain and roughage to provide 10 to 30 grams per ton for cattle and 20 to 30 grams per ton for sheep in the complete feed.

b. Liquid supplements intended for addition to dry feeds

(1) Supplements with suspending agents should be in a pH range of 4-8 and maintain positional stability for up to three months with a viscosity not less than 300 cps.
(2) Conventional liquid supplements should be in a pH range of 4-8. Ten minute recirculation required daily and prior to use.

B. Pasture cattle (slaughter, feeder cattle, and dairy and beef replacement heifers) - For increased rate of weight gain and for control of coccidiosis caused by *Eimeria bovis* and *E. zuernii*.

Feeding directions

For increased rate of weight gain:
Feed at the rate of not less than 60 mg nor more than 300 mg per head per day. Daily lasalocid intakes in excess of 200 mg/head/day have not been shown to be more effective than 200 mg lasalocid/head/day.

For control of coccidiosis:

Feed continuously at the rate of 1 mg of lasalocid per 2.2 pounds of body weight per day in cattle up to 800 pounds (maximum 300 mg per day).

1. Feeds and supplements requiring no further dilution before use

a. Intermediate Blending: Mix 1 part of Bovatec 150 FP premix (Type A Medicated Article) with 29 parts of finely ground non-medicated feedstuffs to provide an intermediate premix containing 5 grams of lasalocid per pound.
b. Final blending: See table below:

In feeds or supplements fed at the rate of: lb/head/day	Feedstuffs a lasalocid intake of: mg/head/day	Add the following amounts of 5 grams per pound intermediate premix per ton of feed or supplement mixed:	Lasalocid will be present in the feed or supplement at the following concentrations: grams/ton
1	60	24	120
	100	40	200
	200	80	400
	300	120	600
2	60	12	60
	100	20	100
	200	40	200
	300	60	300
3	60	8	40
	100	13.3	66.5
	200	26.7	133.5
	300	40	200
4	60	6	30
	100	10	50
	200	20	100
	300	30	150

2. Supplements requiring further dilution before use

Sufficient non-medicated feedstuffs must be thoroughly mixed with the supplement in accordance with the feeding rates listed in section B.1.b above.

a. Intermediate blending: Mix 1 part of Bovatec 150 FP premix (Type A Medicated Article) with 6.5 parts of finely ground non-medicated feedstuffs to provide an intermediate premix containing 20 grams of lasalocid per pound. For example, mix one 50 lb bag of Bovatec 150 FP premix with 325 lb of non-medicated feedstuffs.
b. Using this intermediate premix, the following table would apply to the manufacture of various supplements:

Intended lasalocid concentration in the supplement:	Add the following amounts of 20 grams per pound intermediate premix per ton of supplement mixed:
gram/ton	pound/ton
400	20
600	30
800	40
1000	50
1200	60
1440	72

3. Free choice feed-add supplements

Free choice supplements must be formulated to provide not less than 60 mg nor more than 300 mg of lasalocid per head per day. (Manufacture of Type C free-choice feeds from this product requires a Medicated Feed License Application approved by FDA.)

Caution

Do not allow horses or other equines access to premixes or supplements containing lasalocid, as ingestion may be fatal. The safety of lasalocid in unapproved species has not been established. Feeding undiluted or mixing errors resulting in excessive concentrations of lasalocid could be fatal to cattle and sheep.

Warning

When mixing and handling lasalocid premix, use protective clothing, impervious gloves and a dust mask. Avoid contact with eyes. Operators should wash thoroughly with soap and water after handling. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

NOTE: Coccidiosis may occur when young pasture cattle are co-mingled with adult cattle passing oocysts.

WARNING: Must be thoroughly mixed in feeds before use. Bovatec® 150 FP premix should be further diluted before mixing in complete feed.

NADA 95-298, Approved by FDA

ALPHARMA

Alpharma Inc.

One Berkeley Drive

Bedford, New Jersey 07004

Net wt 50 LB (22.68 kg)

Take Time

Observe Label

Directions

Made in USA

710316 0105

000000

List No. 710127

Control

Expires:

**Type A Medicated Article** (medicated premix)**Brand of lasalocid**

CATTLE: For improved feed efficiency and increased rate of weight gain when used in medicated feeds for cattle fed in confinement for slaughter. For increased rate of weight gain when used in medicated feeds for pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers).

For control of coccidiosis caused by *Eimeria bovis* and *E. zuernii* in cattle up to 800 lbs.

SHEEP: For prevention of coccidiosis caused by *Eimeria ovina*, *E. crandallis*, *E. ovinoidalis* (*E. ninakohlyakimovae*), *E. parva* and *E. intricata* in sheep maintained in confinement.

Each pound contains 90.7 grams (20%) of lasalocid (as lasalocid sodium activity) in a carrier suitable for incorporation in liquid feed supplements.

IMPORTANT: Must be thoroughly mixed in feeds before use.

DO NOT FEED UNDILUTED

Net Wt. 50 Lb. (22.68 kg)

NADA 95-298, Approved by FDA



Alpha Inc.
One Executive Drive, Fort Lee, New Jersey 07024

See side panel for use directions



Made in the U.S.A. ABL-Z95 0105

USE DIRECTIONS:
A. FEEDLOT CATTLE BEING FED IN CONFINEMENT FOR SLAUGHTER - FOR IMPROVED FEED EFFICIENCY AND INCREASED RATE OF WEIGHT GAIN AND FOR CONTROL OF COCCIDIOSIS CAUSED BY *Eimeria bovis* AND *E. zuernii*.

SHEEP - FOR PREVENTION OF COCCIDIOSIS CAUSED BY *Eimeria ovina*, *E. crandallis*, *E. ovinoidalis* (*E. ninakohlyakimovae*), *E. parva* AND *E. intricata* IN SHEEP MAINTAINED IN CONFINEMENT.

FEEDING DIRECTIONS:

FOR IMPROVED FEED EFFICIENCY IN CATTLE: Feed continuously at the rate of not less than 10 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 100 mg nor more than 360 mg per head per day.

FOR IMPROVED FEED EFFICIENCY AND INCREASED RATE OF WEIGHT GAIN IN CATTLE: Feed continuously at the rate of not less than 25 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 250 mg nor more than 360 mg per head per day.

FOR CONTROL OF COCCIDIOSIS IN CATTLE: Feed continuously at the rate of 30 grams of lasalocid per ton of total ration (90% dry matter) to provide an intake of 1 mg of lasalocid per 2.2 pounds of body weight per day in cattle up to 800 pounds (maximum 360 mg per day).

FOR PREVENTION OF COCCIDIOSIS IN SHEEP: Feed continuously at the rate of not less than 20 grams nor more than 30 grams of lasalocid per ton of total ration (90% dry matter) to provide not less than 15 mg nor more than 70 mg per head per day depending on body weight.

B. PASTURE CATTLE (SLAUGHTER, STOCKER, FEEDER CATTLE, AND DAIRY AND BEEF REPLACEMENT HEIFERS) - FOR INCREASED RATE OF WEIGHT GAIN AND FOR CONTROL OF COCCIDIOSIS CAUSED BY *Eimeria bovis* AND *E. zuernii*.

FEEDING DIRECTIONS:

FOR INCREASED RATE OF WEIGHT GAIN: Feed at the rate of not less than 60 mg nor more than 300 mg per head per day. Hand-fed: The drug must be contained in at least one pound of feed. Self-fed: Free-choice feed must be manufactured under a feed mill license utilizing an FDA approved formulation. Daily lasalocid intakes in excess of 200 mg/head/day have not been shown to be more effective than 200 mg lasalocid/head/day.

FOR CONTROL OF COCCIDIOSIS: Hand feed continuously at the rate of 1 mg of lasalocid per 2.2 pounds of body weight per day in cattle up to 800 pounds (maximum 360 mg per day).

MIXING DIRECTIONS - for incorporation into liquid feed supplements:

- (1) Agitate Bovatec Liquid 20 before use.
- (2) Supplements with suspending agent(s) should be in a pH range of 4 - 8 and maintain positional stability for up to three months with a viscosity not less than 300 cps.
- (3) Conventional liquid supplements should be in a pH range of 4 - 8. Ten minute recirculation required daily and prior to use.

The following is provided as a guide in determining the quantity of Bovatec Liquid 20 (Type A Medicated Article) to be added in preparing liquid feed supplements (LFS). Preparation of intermediate liquid premix is not recommended.

LFS TO BE FED UNDILUTED

As a Type C Medicated Feed - Hand-Fed or Top Dressed

Amount of LFS to be fed (Lb./Head/Day)	To achieve a lasalocid intake of (Mg/Head/Day)	Bovatec Liquid 20 per Ton LFS	
		Pounds	Fluid Ounce*
0.5	15	0.67	3.5
0.5	60	2.65	39.2
0.5	70	3.09	45.7
0.5	100	4.41	65.6
0.5	200	8.83	130.6
0.5	360	15.88	235.0
1.0	15	3.4	4.9
1.0	60	1.33	19.6
1.0	70	1.55	22.9
1.0	100	2.23	32.7
1.0	200	4.41	65.3
1.0	360	7.94	117.5

LFS TO BE DILUTED

As a Type B Medicated Feed - Mixed into a Feed

Amount of LFS to be added to final feed (Lb./Ton)	Lasalocid in final feed (Gram/Ton)	Bovatec Liquid 20 per Ton LFS	
		Pounds	Fluid Ounce*
100	10	2.21	32.7
100	20	4.42	65.3
100	25	5.52	81.6
100	30	6.62	97.9
150	10	1.68	21.8
150	20	2.96	43.6
150	25	3.68	54.4
150	30	4.42	65.3
200	10	1.11	16.4
200	20	2.21	32.7
200	25	2.76	40.8
200	30	3.31	49.0

* 6.13 gm lasalocid per fluid ounce (Bovatec Liquid 20 specific gravity is 1.035)

NOTE: Coccidiosis may occur when young pasture cattle are co-mingled with adult cattle passing coccidial oocysts. **CAUTION:** Do not allow horses or other equines access to premises or supplements containing lasalocid, as ingestion may be fatal. The safety of lasalocid in unapproved species has not been established. Feeding undiluted or mixing errors resulting in excessive concentrations of lasalocid could be fatal to cattle and sheep.

WARNING: When mixing and handling lasalocid liquid premix, use protective clothing and impervious gloves. Avoid contact with eyes. Operators should wash thoroughly with soap and water after handling. A withdrawal period has not been established for this product in pre-ruminating calves.

Do not use in calves to be processed for veal.

Lot _____

**Blue Bird Lasalocid
Cattle Hand-Fed Supplement
Type C Feed
MEDICATED**

For increased rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers).

ACTIVE DRUG INGREDIENT

Lasalocid (as lasalocid sodium)..... g/ton

GUARANTEED ANALYSIS

Crude Protein, not less than	_____ %
Crude Protein from non-protein nitrogen (NPN) ¹ , not more than	_____ %
Crude Fat, not less than	_____ %
Crude Fiber, not more than	_____ %
Calcium, not less than	_____ %
Calcium, not more than	_____ %
Phosphorus, not less than	_____ %
Salt ¹ , not less than	_____ %
Salt ¹ , not more than	_____ %
Potassium, not less than	_____ %
Vitamin A ¹ , not less than	_____ IU/lb

¹If added.

INGREDIENTS

Ingredients as defined by AAFCO.

FEEDING DIRECTIONS

Feed continuously on a hand-fed basis at a rate of not less than 60 mg nor more than 300 mg of lasalocid per head per day. The drug must be contained in at least 1 lb of feed. Daily intakes of lasalocid in excess of 200 mg/head/day have not been shown to be more effective than 200 mg/head/day.

CAUTION

The safety of lasalocid in unapproved species has not been established. Do not allow horses or other equines access to supplements containing lasalocid as ingestion may be fatal.

WARNING

A withdrawal period has not been established for this product in pre-ruminating cattle. Do not use in calves to be processed for veal.

NET WEIGHT ON BAG OR BULK

**BLUE BIRD FEED MILLS
Any Town, USA 12345**

Lot _____

Blue Bird Lasalocid - M
Cattle Free-Choice Mineral and Vitamin Supplement
Type C Feed
MEDICATED

For increased rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers).

ACTIVE DRUG INGREDIENT

Lasalocid (as lasalocid sodium).....1440 g/ton

GUARANTEED ANALYSIS

Calcium, not less than	_____ %
Calcium, not more than	_____ %
Phosphorus, not less than	_____ %
Salt ¹ , not less than	_____ %
Salt ¹ , not more than	_____ %
Magnesium, not less than	_____ %
Potassium, not less than	_____ %
Copper, not less than	_____ %
Selenium, not less than	_____ %
Zinc, not less than	_____ %
Vitamin A ¹ , not less than	_____ IU/lb

¹If added.

INGREDIENTS

Ingredients as defined by AAFCO.

FEEDING DIRECTIONS

Feed continuously on a free-choice basis. Pasture and roughage should be adequate to assure consumption of Blue Bird Lasalocid - M will be 1.34 to 6.66 oz/head/day (which provides for 60 to 300 mg lasalocid). If cattle consume more or less than these amounts, try moving feeder further or closer to the general resting or water areas. Daily intakes of lasalocid in excess of 200 mg/head/day (4.44 oz/head/day of Blue Bird Lasalocid - M) have not been shown to be more effective than 200 mg/head/day.

CAUTION

The safety of lasalocid in unapproved species has not been established. Do not allow horses or other equines access to supplements containing lasalocid as ingestion may be fatal.

WARNING

A withdrawal period has not been established for this product in pre-ruminating cattle. Do not use in calves to be processed for veal.

NET WEIGHT ON BAG OR BULK

BLUE BIRD FEED MILLS
 Any Town, USA 12345

* Feed Mill License required for free-choice feeds.

Blue Bird Lasalocid – L
Cattle Free-Choice Liquid Supplement
Liquid Type C Feed
MEDICATED

For increased rate of weight gain in pasture cattle (slaughter, stocker, feeder cattle, and dairy and beef replacement heifers).

ACTIVE DRUG INGREDIENT

Lasalocid (as lasalocid sodium) 150 g/ton

GUARANTEED ANALYSIS

Crude Protein, not less than	_____ %
Crude Protein from non-protein nitrogen (NPN) ¹ , not more than	_____ %
Crude Fat, not less than	_____ %
Crude Fiber, not more than	_____ %
Calcium, not less than	_____ %
Calcium, not more than	_____ %
Phosphorus, not less than	_____ %
Salt ¹ , not less than	_____ %
Salt ¹ , not more than	_____ %
Potassium, not less than	_____ %
Vitamin A, not less than	_____ IU/lb

¹If added.

INGREDIENTS

Ingredients as defined by AAFCO.

FEEDING DIRECTIONS

Once cattle have been acclimated to a non-medicated free-choice liquid supplement, approximately 14 days, feed continuously on a free-choice basis. Pasture and roughage should be adequate to assure consumption of supplement will be 0.8 to 4.0 lbs/head/day (which provides 60 to 300 mg lasalocid). If cattle consume more or less than these amounts, try (1) moving feeder further or closer to the general resting or water area; or (2) increasing or decreasing number of animals per wheel; or (3) utilize lick wheel limiter to regulate wheel exposure – increasing exposure to increase consumption or decreasing exposure to decrease consumption, making certain wheel turns freely after each adjustment. Daily intakes of lasalocid in excess of 200 mg/head/day (2.67 lbs/head/day of Blue Bird-L) have not been shown to be more effective than 200 mg/head/day.

CAUTION

The safety of lasalocid in unapproved species has not been established. Do not allow horses or other equines access to supplements containing lasalocid as ingestion may be fatal.

WARNING

A withdrawal period has not been established for this product in pre-ruminating cattle. Do not use in calves to be processed for veal.

NET WEIGHT

BLUE BIRD FEED MILLS
 Any Town, USA 12345

Expires: _____ (Two months after manufacture)

* Feed Mill License required for free-choice feeds.